



OBLON ET AL (703) 413-3000  
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INV. Jacques THEZE ET AL.  
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DATED 06/28/2004  
REPLACEMENT DRAWINGS

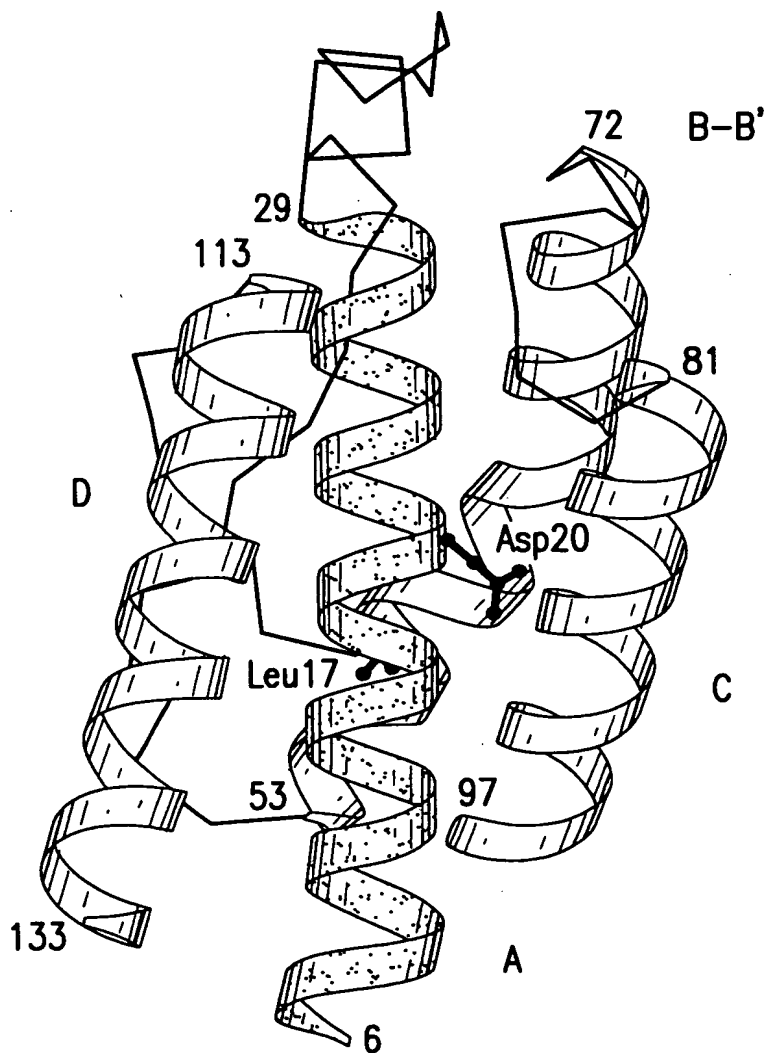
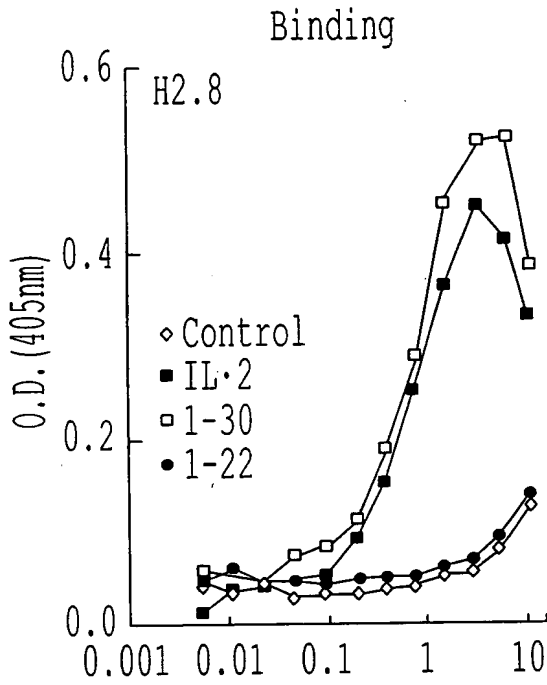
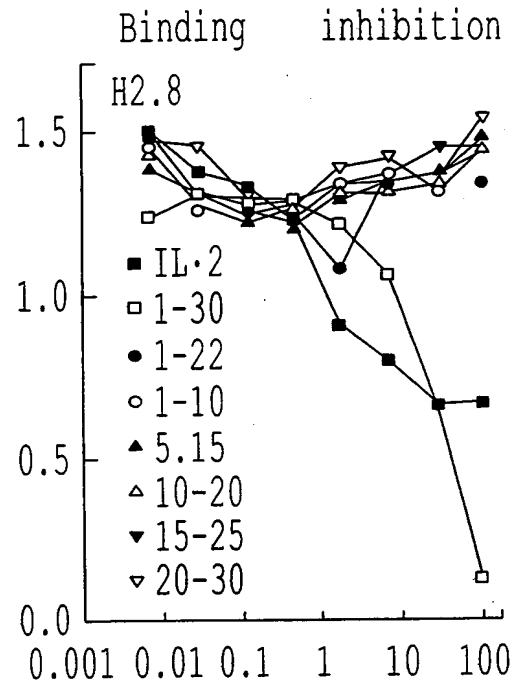


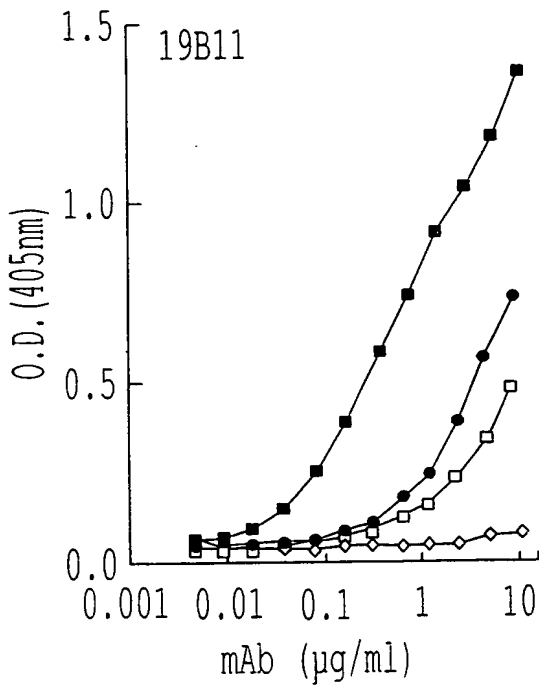
FIG. 1



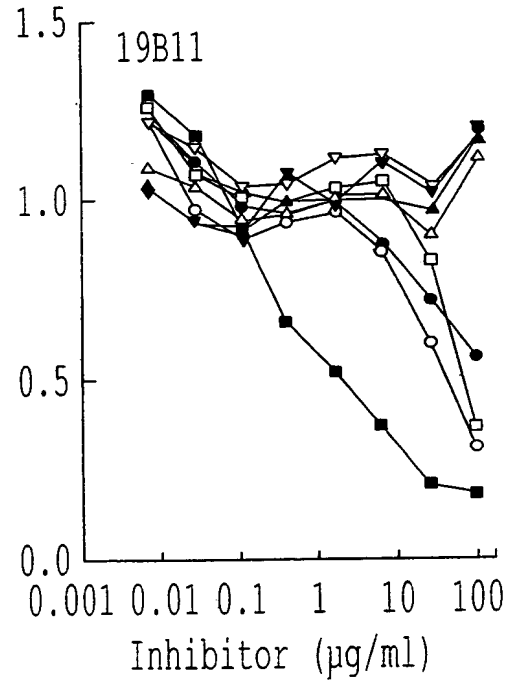
*FIG. 2*



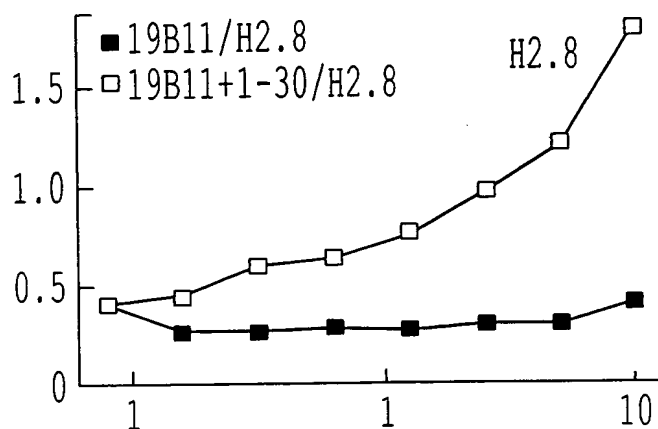
*FIG. 2*



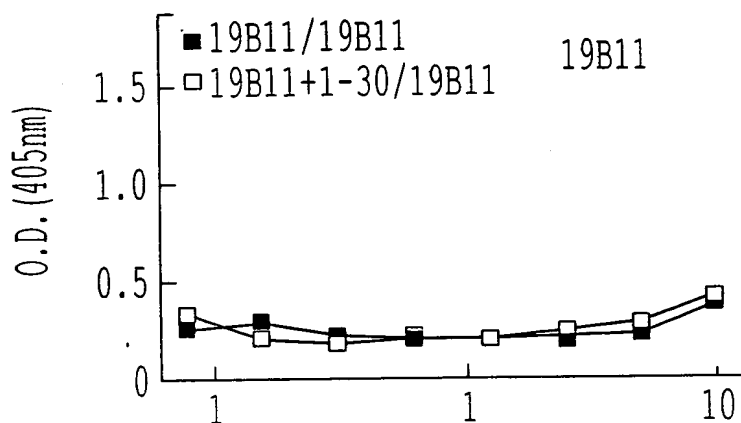
*FIG. 2*



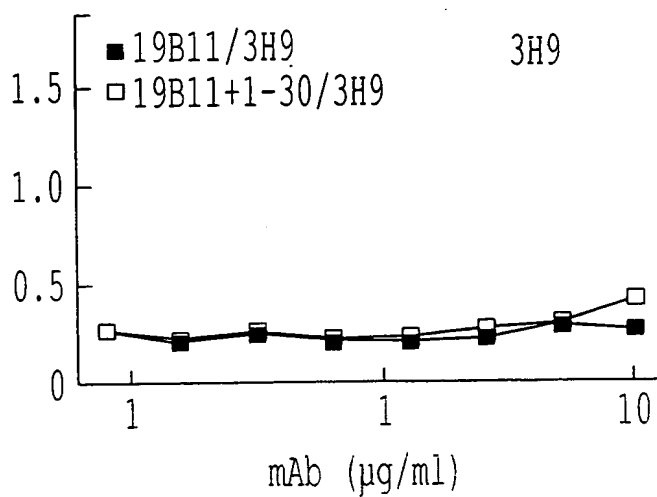
*FIG. 2*



*FIG. 3*



*FIG. 3*



*FIG. 3*

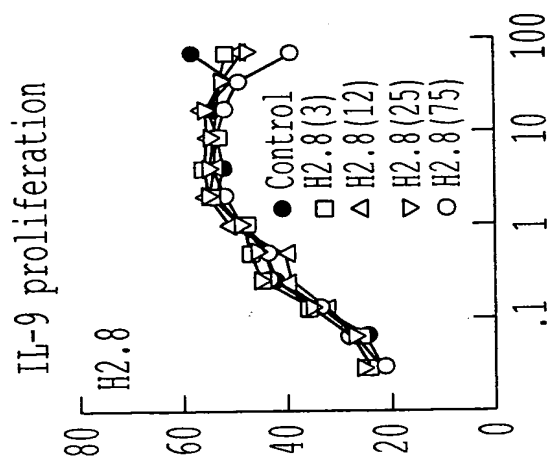


FIG. 4

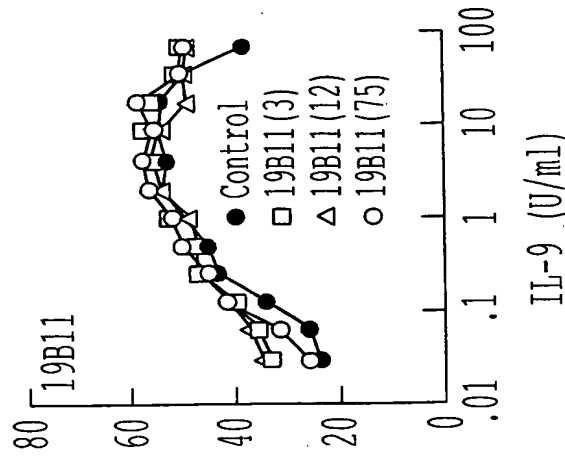


FIG. 4

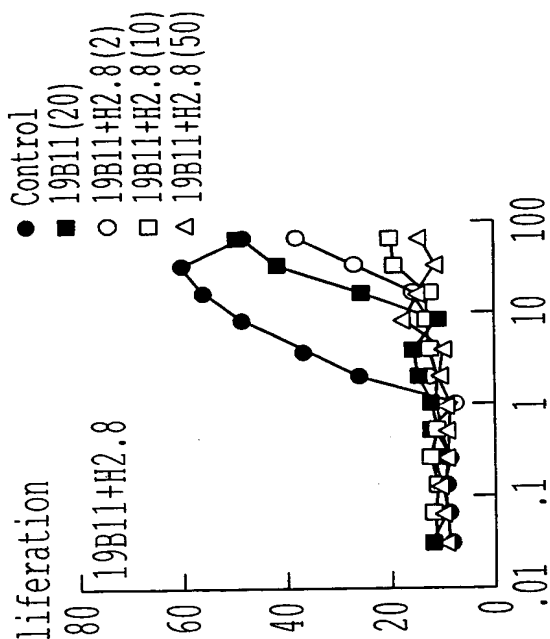


FIG. 4

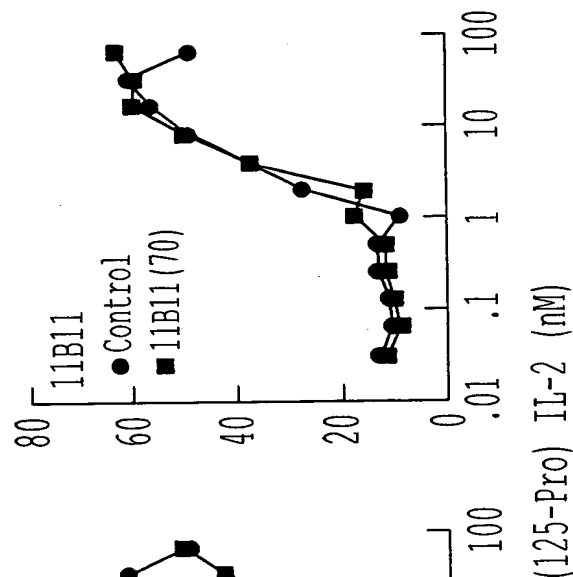


FIG. 4

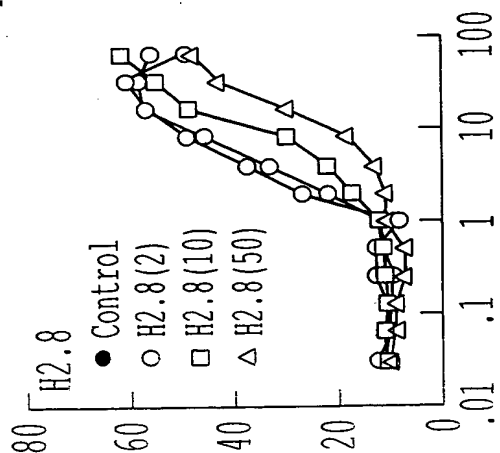


FIG. 4

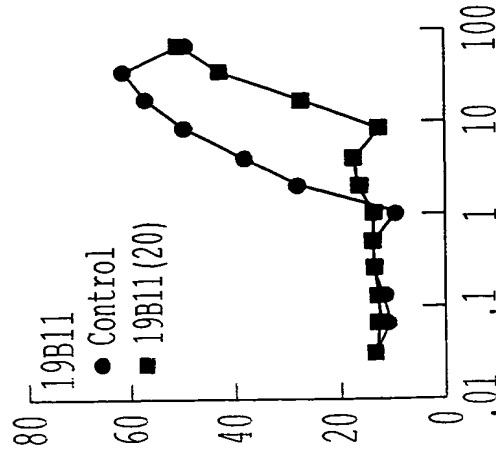


FIG. 4

$[^3\text{H}]\text{TdR}$  incorporation ( $\times 10^{-3}$ )

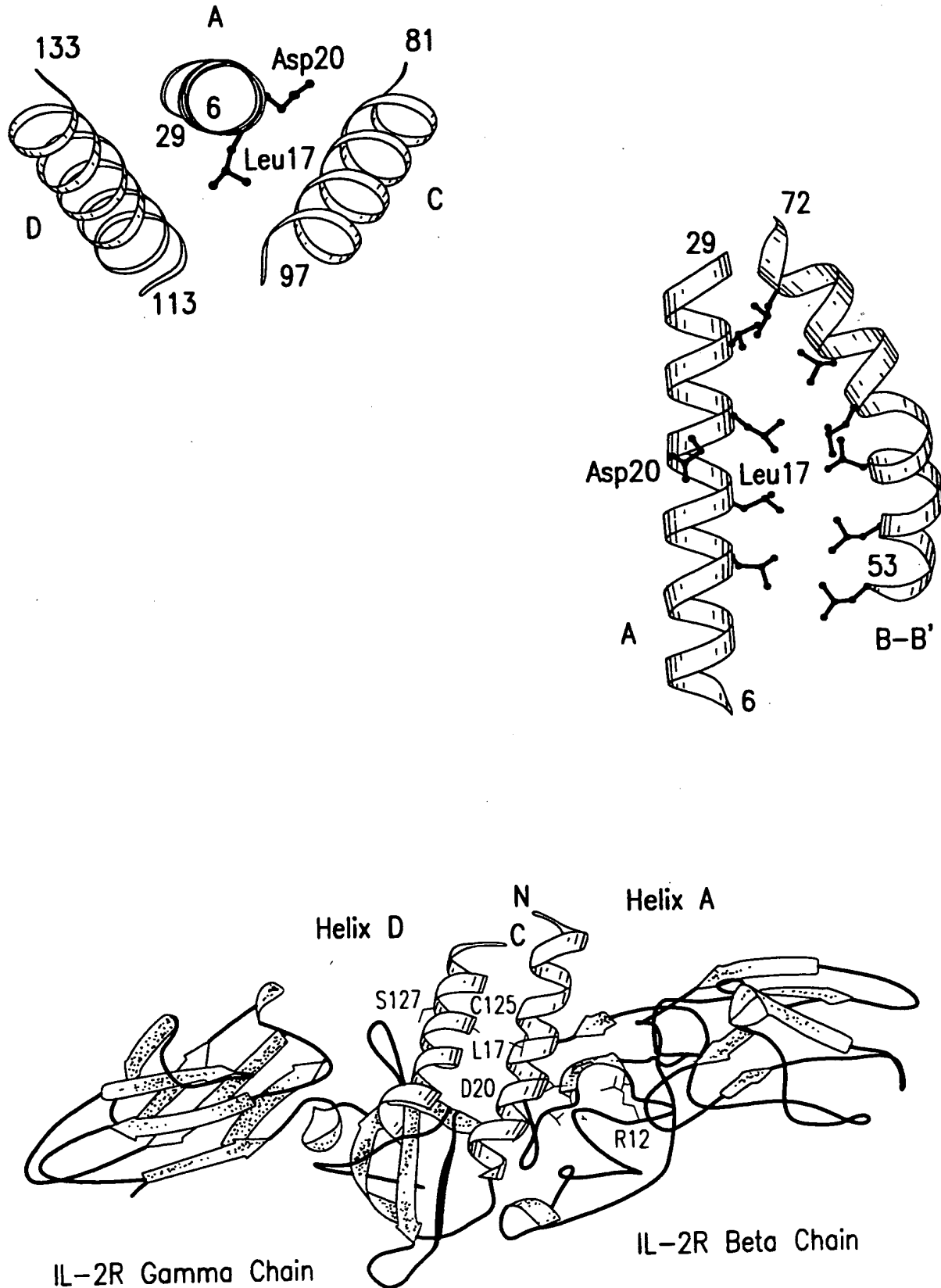


FIG.5

Interleukine-2 receptor

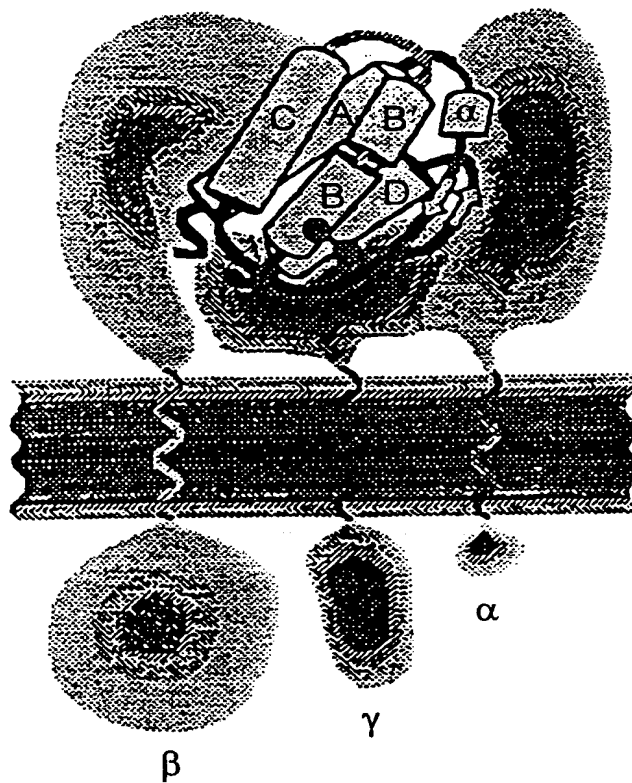


FIG.6

IL-2 AND IP130 SEQUENCE ( $\alpha$ -HELICES ARE BOXED)

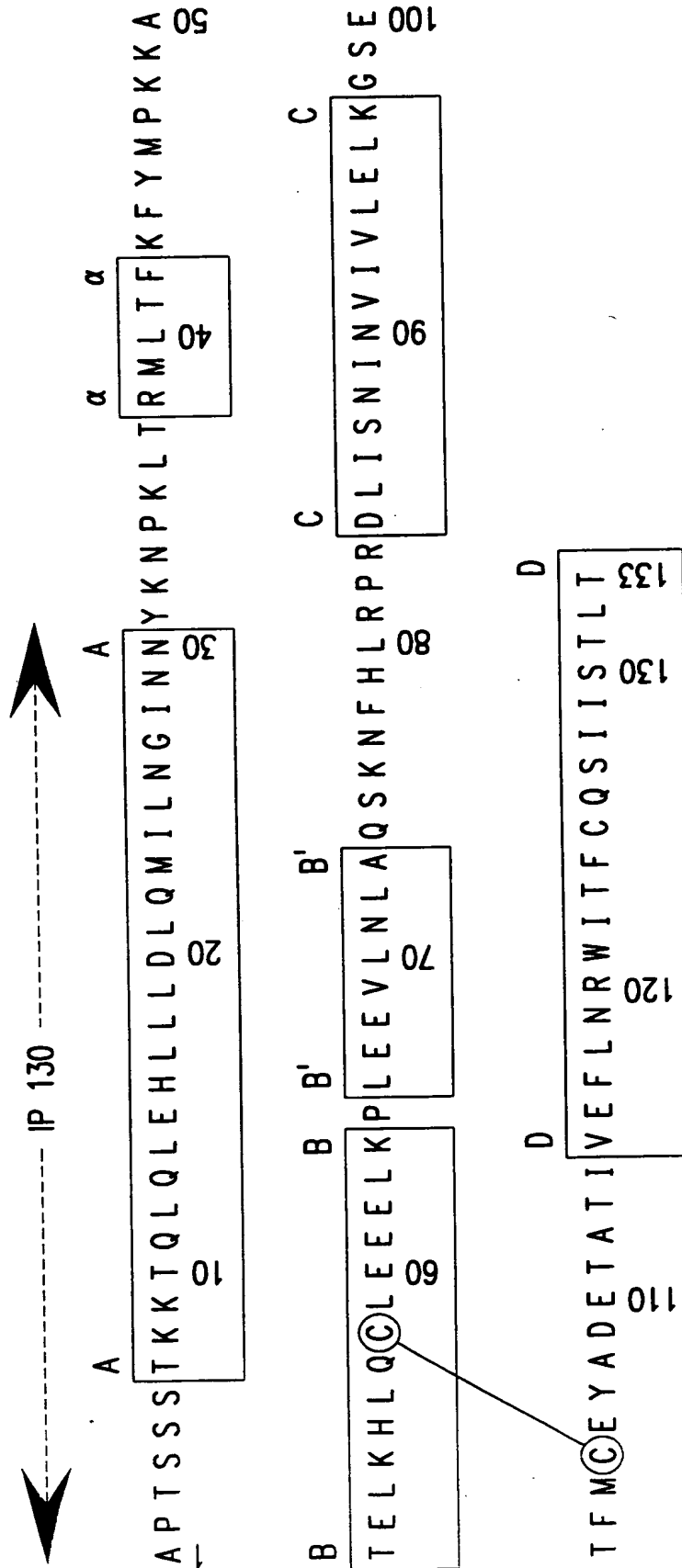
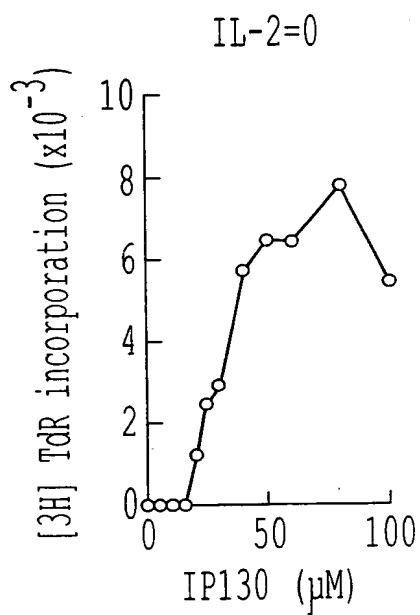
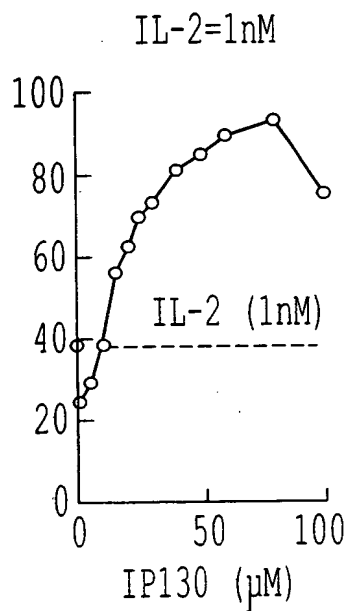


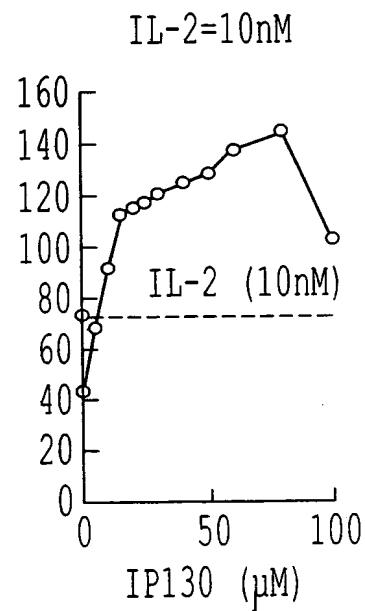
FIG.6



**FIG. 7**

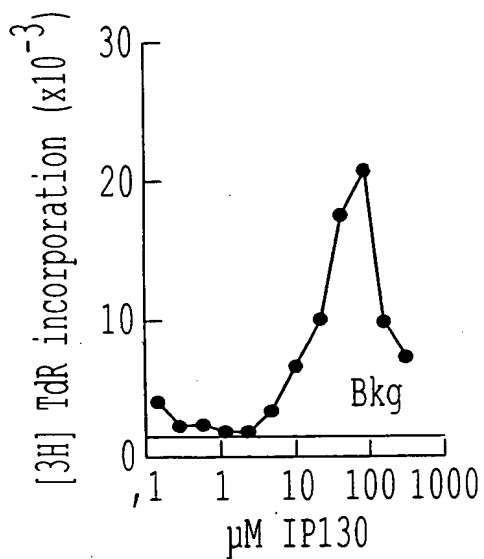


**FIG. 7**

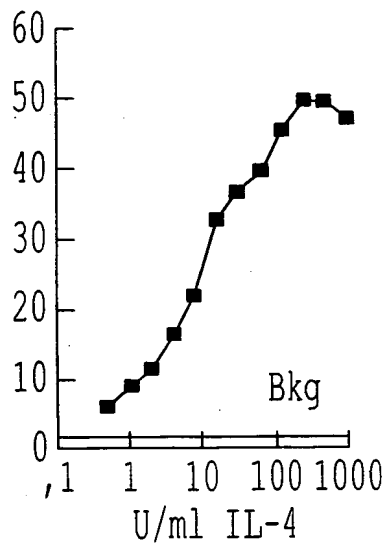


**FIG. 7**

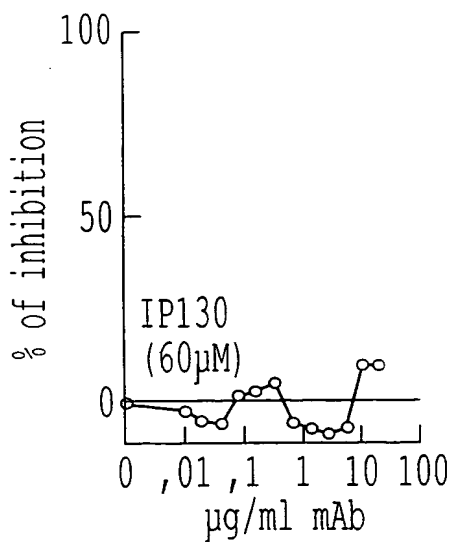




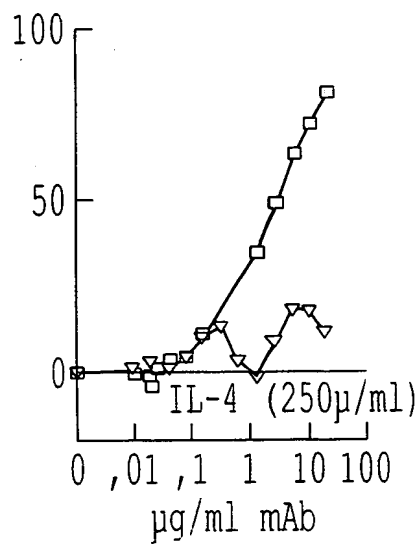
**FIG. 8A**



**FIG. 8B**



**FIG. 8C**



**FIG. 8C**

● IL-4  
○ IL-4 IP130

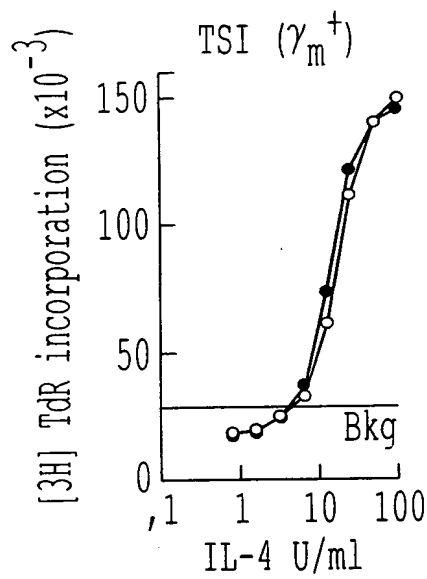


FIG. 9A

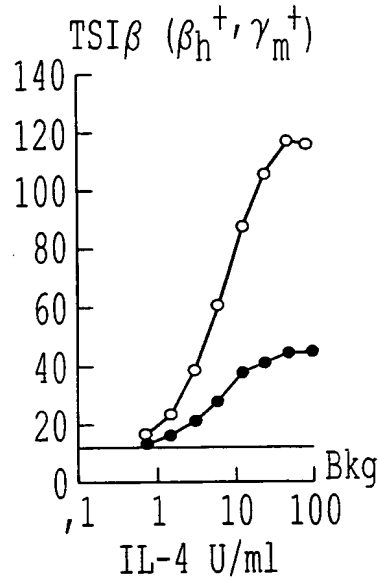


FIG. 9A

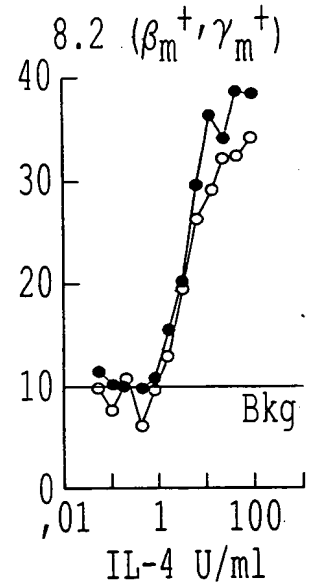


FIG. 9A

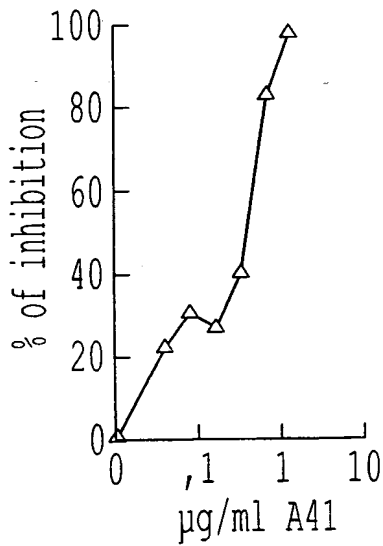


FIG. 9B

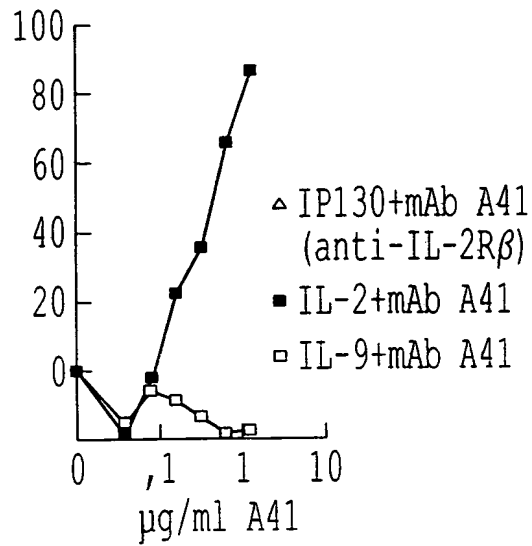


FIG. 9B

1 10 20 30  
 APTTSSSTKKTQLQLEHLLLDLQMILNGINN

% helix  
 (Circular dichroism)

Main molecular species

Activity



Telramer (4M-8M, Kd=30-100µM)  
 /Octamer

+++  
 ++



Dimer (1M-2M, Kd=0, 2µM)  
 /Telramer (2M-4M, Kd=100µM)

-

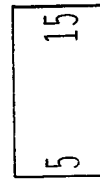


<2%



Dimer (1M-2M, Kd=50µM)  
 (2M-4M, Kd=1, 4mM)

-



0%

Dimer (1M-2m, Kd=113µM)

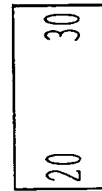
-



0%

Monomer

ND

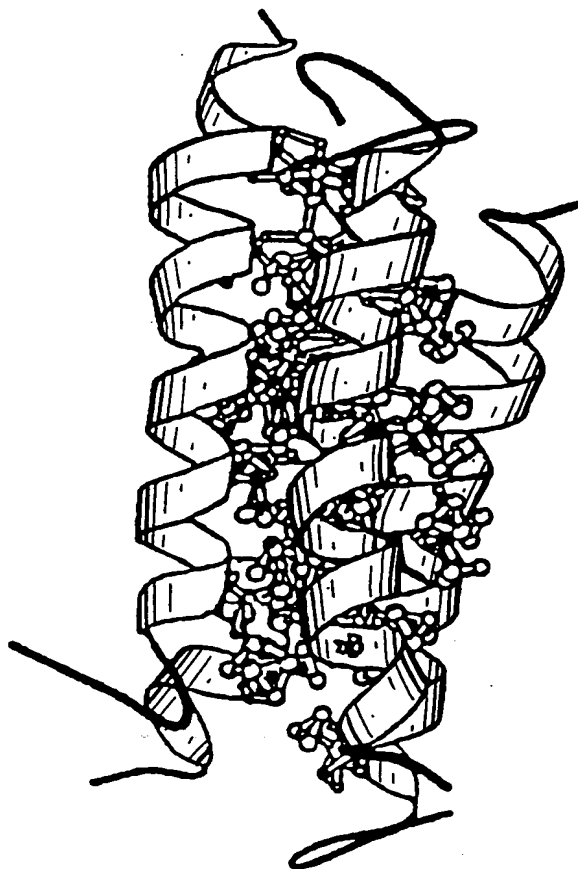


<5%

Monomer

+

FIG. 10



IP130

FIG.11

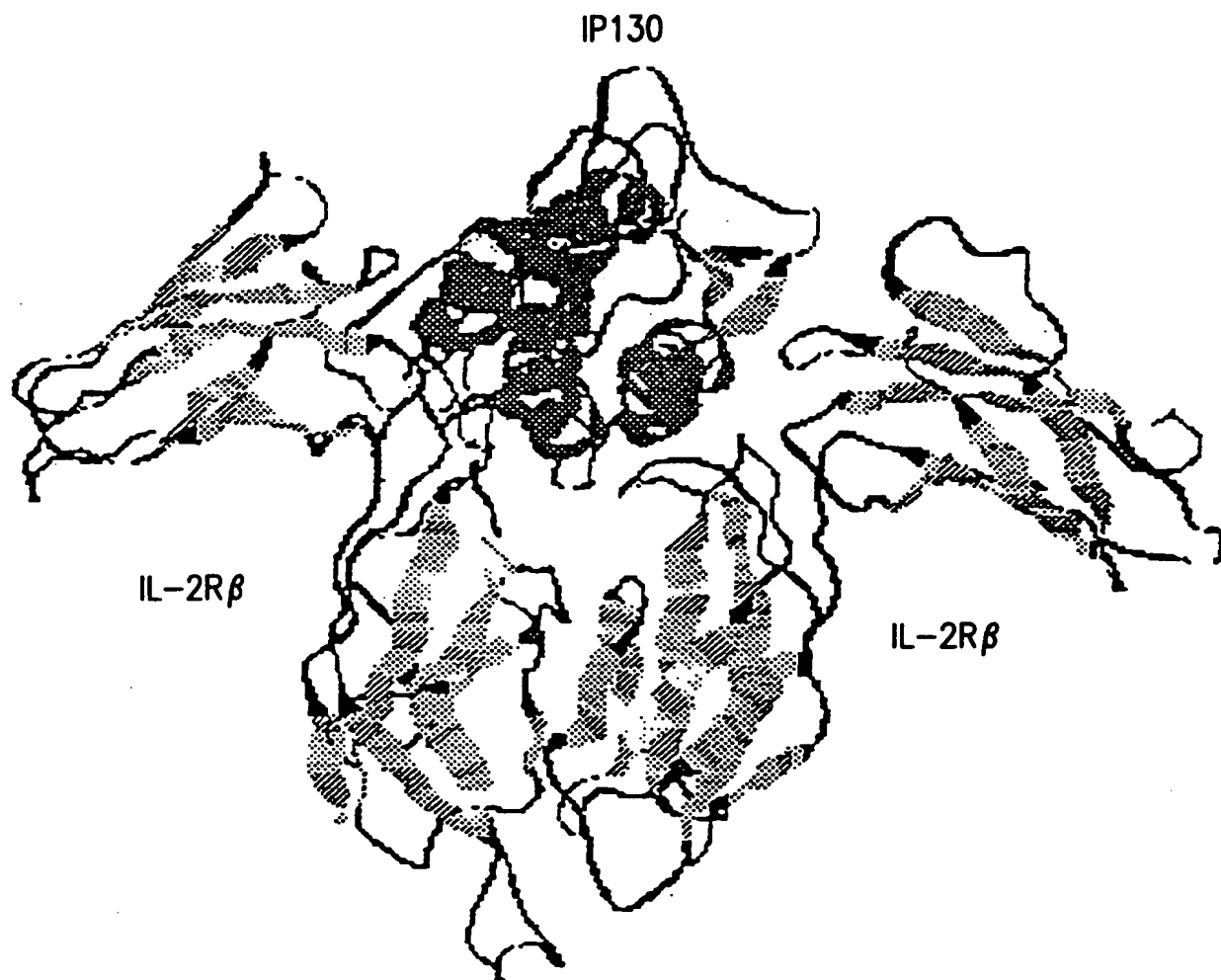
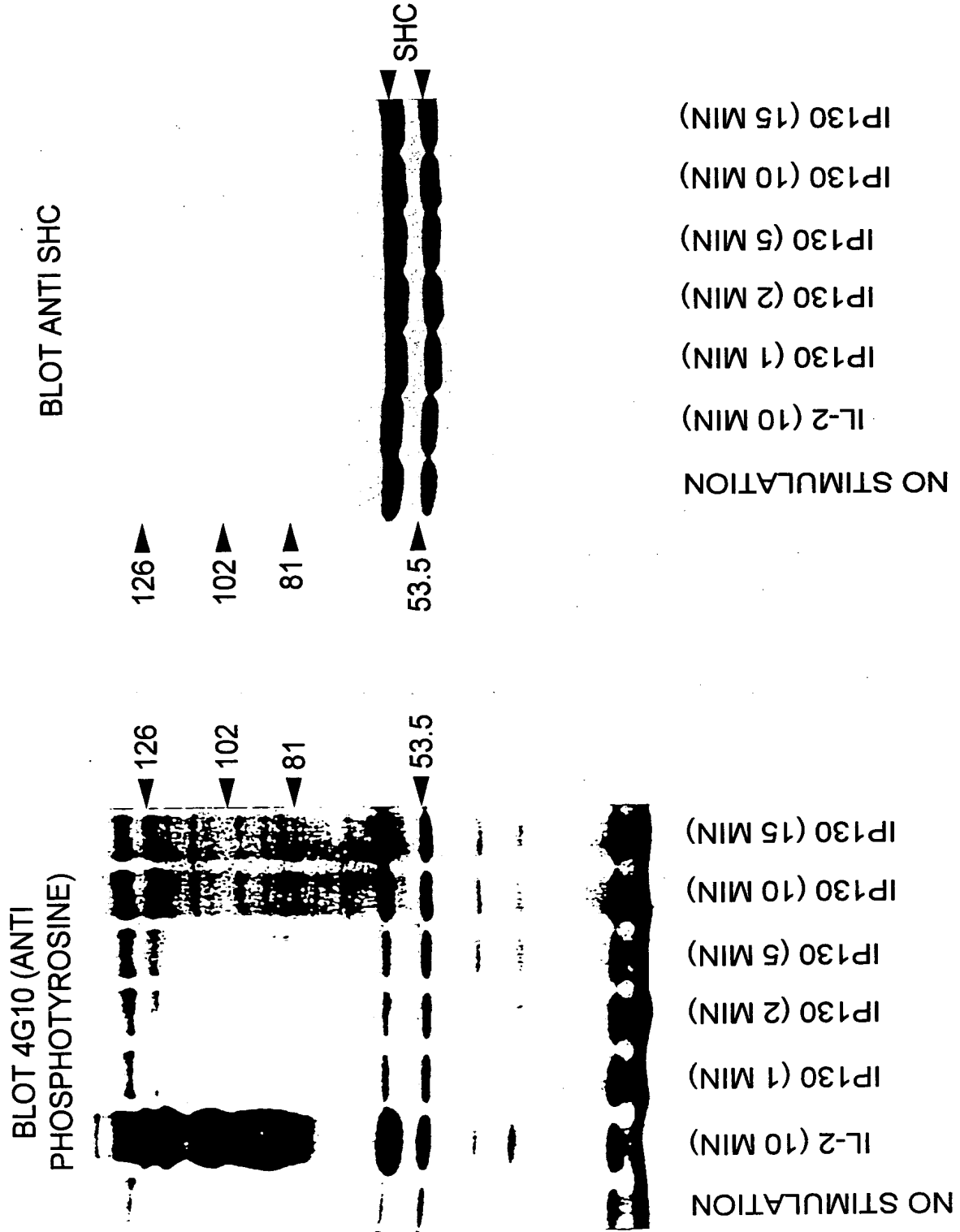


FIG. 11



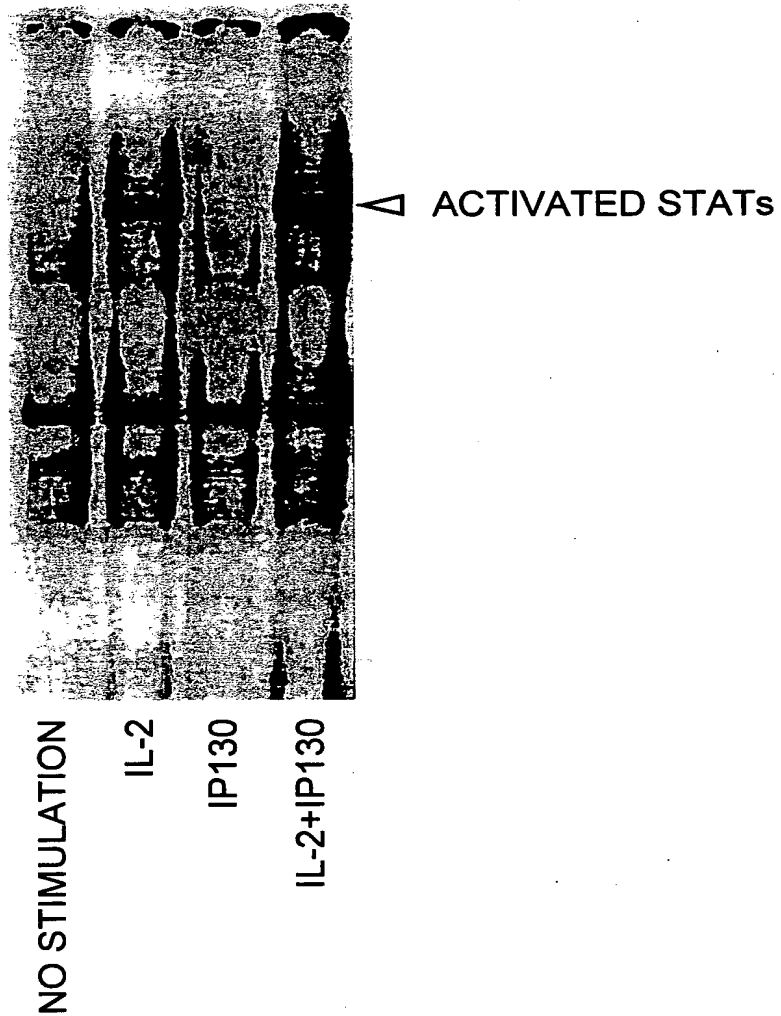
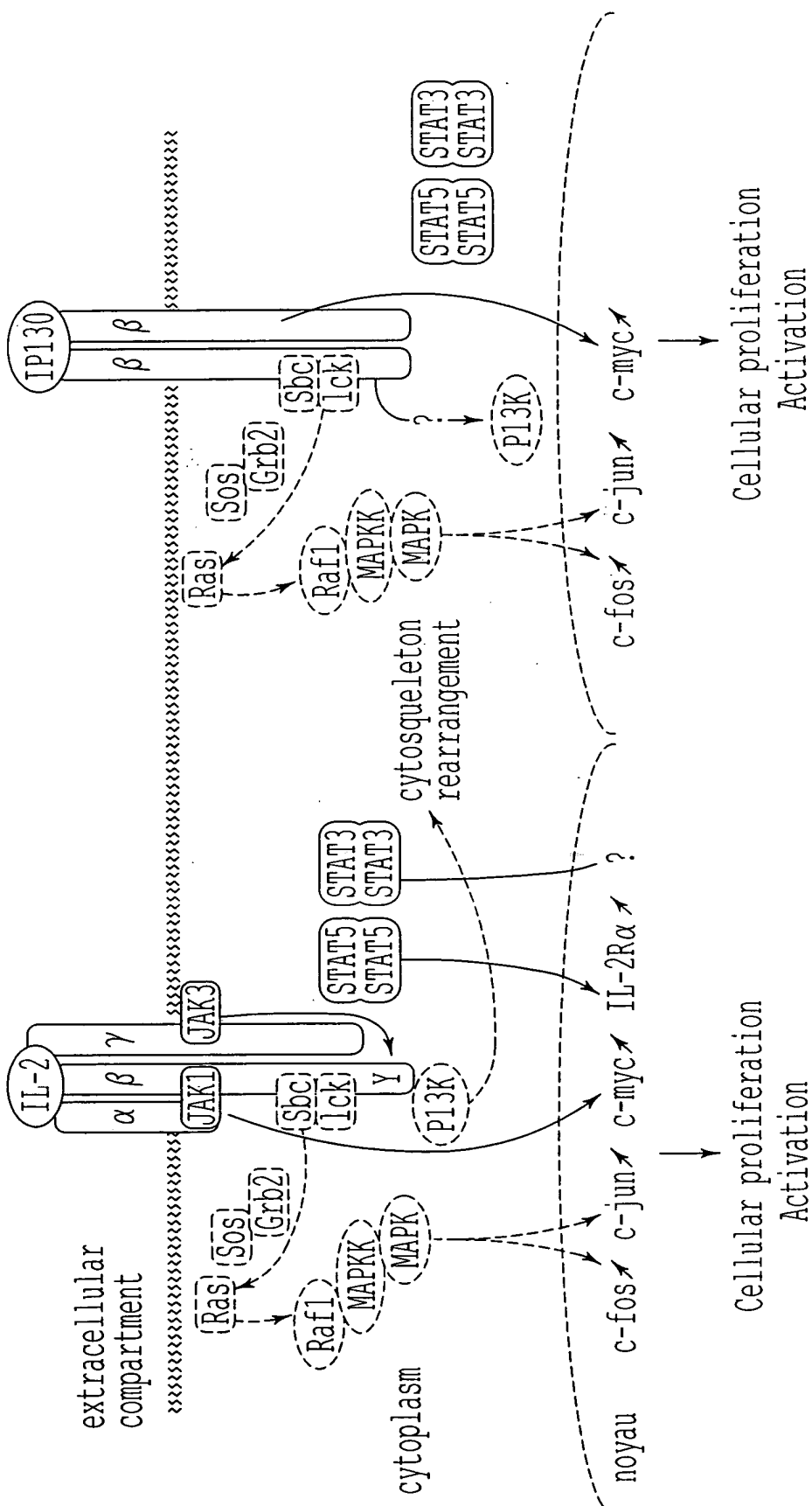


FIG.13



IL-2 receptor and its major signal transduction pathway Model of transduction pathway induced by IP130

FIG. 14



NK cells (CD56<sup>+</sup>) entering in S+G2/M phases after IP130 stimulation  
(synergy with IL-2)

Treatment		J31	J32	J33
IL-2 50 nM		14	12	14
	IP130 60 $\mu$ M	0	17	$\leq 5$
	IP130 120 $\mu$ M	0	14	$< 5$
IL-2 50 nM +	IP130 60 $\mu$ M	26	21	7
IL-2 50 nM +	IP130 120 $\mu$ M	28	28	28

*FIG. 15*

Stimulation  
 3 Days

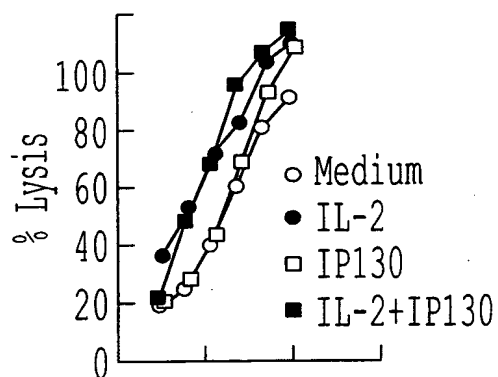


FIG. 16

Effector / target=10

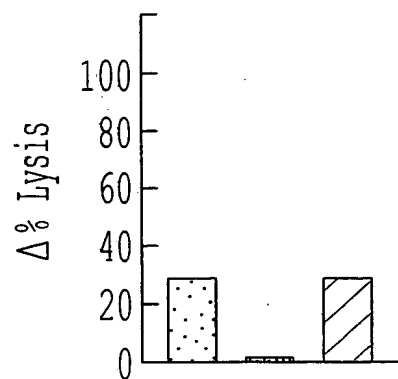


FIG. 16

6 Days

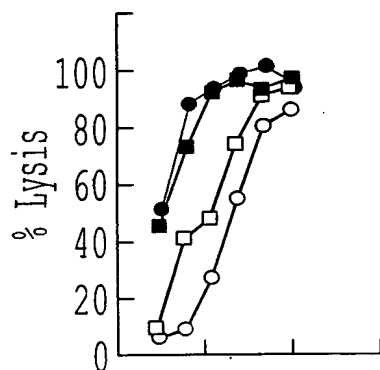


FIG. 16

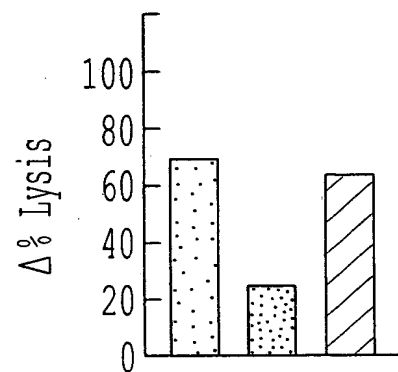


FIG. 16

9 Days

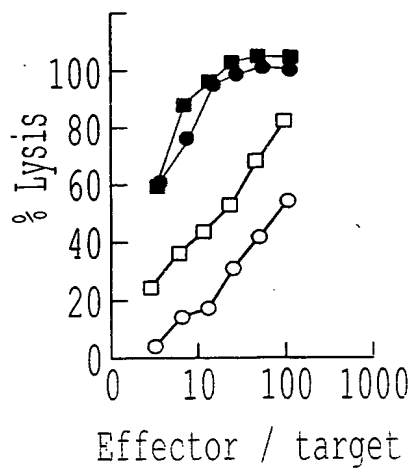


FIG. 16

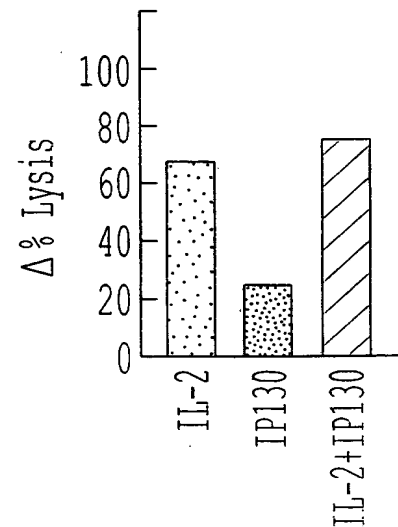


FIG. 16